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ORIGINAL ARTICLE

Does transcranial stimulation for motor evoked potentials (TcMEP) worsen seizures in epileptic patients following spinal deformity surgery?

Khalid M. I. Salem[1] · Laura Goodger[1] · Katherine Bowyer[1] · Masood Shafafy[1] · Michael P. Grevitt[1]

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Abstract
Purpose To investigate the effect of Transcranial Motor Evoked Potentials (TcMEP) in increasing the severity or frequency of post-operative seizures in patients undergoing deformity corrective spine surgery with a known history of seizures pre-operatively.
Methods The information on all patients with history of epilepsy/seizures who underwent spinal TcMEP cord monitoring for deformity correction surgery was retrospectively collected through a review of the hospital notes. The benefits of TcMEP in the early detection of potential cord ischemia were deemed by the operating surgeon to outweigh the increased risks of seizures, tongue biting, etc. Data on age, gender, pre-operative diagnosis, curve type, intra-operative monitoring alerts, duration of hospital stay, and post-operative in-hospital seizures were collected. Additionally, the patients were contacted following discharge and data on any change in the frequency of the seizures or an alteration in seizure-related medication post-operatively was also collected.
Results The records of 449 consecutively monitored patients were reviewed and 12 (2.7 %) patients with a history of seizures pre-operatively were identified. The mean age was 23 (9–59) years, 7 females, 11 scoliosis corrections (4 neuromuscular, 1 degenerative, 6 idiopathic adolescent), and one sagittal balance correction surgery. Intra-operatively, all patients had TcMEP monitoring, were catheterised, and had no neuromonitoring alerts or record of tongue biting or laceration. Post-operatively, the mean hospital stay was 12 (4–25) days with no recorded seizures. At a mean of 23 (12–49) months post-discharge, none of the patients reported a worsening of seizures (pattern or frequency) or required an alteration in the seizure-related medications.
Conclusion TcMEP does not appear to trigger intra-operative or post-operative seizures and is not associated with deterioration in the seizure control of patients suffering seizures pre-operatively.

Keywords Transcranial motor evoked potential · Epilepsy · Seizure · Intra-operative neuromonitoring

Introduction

Intra-operative neuromonitoring (IONM) serves to detect inadvertent damage early when the resulting dysfunction might still be reversible and provide a guide to the extent of safe operative manipulation (in deformity surgery) or resection (in oncologic surgery). Ideally the monitoring technique should be highly sensitive and specific, provide rapid feedback, and should not intrude into the surgical field or the anesthetist work space [1]. The use of somatosensory evoked potentials (SSEP) preceded the use of transcranial motor evoked potential (TcMEP) by a couple of decades but was shown to be less reliable than TcMEP [2].

For most patients, iatrogenic power loss or paralysis is a more detrimental post-operative complication than sensation loss but concerns relating to the potential for triggering or worsening seizures in predisposed patients limited its use by the spine surgeons in this patient subgroup despite the lack of evidence to back this assumption.

✉ Khalid M. I. Salem
kmsalem@gmail.com

[1] Nottingham University Hospital NHS Trust, Queen's Medical Centre Campus, Centre for Spinal Studies and Surgery, Nottingham NG7 2UH, UK

Through a case series review, we aim to investigate the effect of TcMEP in increasing the severity or frequency of post-operative seizures in patients undergoing deformity corrective spine surgery with a known history of seizures pre-operatively.

Methods

The hospital records of a tertiary spine surgery referral unit [Nottingham—Center for Spinal Studies and Surgery (CSSS)] and intra-operative monitoring data of all patients with a pre-operative history of seizures that had undergone a spinal deformity corrective surgery were retrospectively reviewed. Data on patient's age, gender, pre-operative diagnosis, type of curve, intra-operative monitoring alerts, duration of hospital stay, and medical recording of post-operative in-hospital seizures were collected. A telephone questionnaire was conducted with the patients/their guardians and additional information on changes in seizure frequency and alterations to seizure-related medication post-operatively since discharge from hospital was gathered.

Intra-operative neurological monitoring protocol

To optimize the conditions for IONM we use the total intravenous anesthetic technique (TIVA) that facilitates a constant anesthetic concentration "steady state" for neruomonitoring during surgery. This typically utilizes the intravenous use of Propofol (anesthetic agent), a synthetic narcotic such as Sufentanil, an infusion of the local esthetic Lidocaine and frequently the *N*-methyl D-aspartate (NMDA) receptor antagonist (Ketamine). For induction, all agents are given as a bolus then administered as a continuous infusion to maintain a "steady" concentration intra-operatively. Inhalation anesthetic agents are avoided. An additional neuromuscular blocking agent (which can be depolarizing—such as Succinylcholine or non-depolarizing—such as Rocuronium) might be used to facilitate intubation [3].

We routinely record TcMEPs and SSEPs alternately throughout the procedure except in the rare situation when SSEPs are unrecordable where TcMEPs are then used in isolation. Additionally, a Cerebral Function Analysing Monitor (CFAM) is routinely used intra-operatively to record brain activity over time (frequency and amplitude). This allows monitoring the cerebral changes in response to anesthesia, reduced perfusion, and/or cerebral dysfunction such as seizures.

The IONM during this study was initially carried out using a Nicolet Viking Select in conjunction with a Digitimer D185 external MEP voltage stimulator for the majority of cases. The purchase of an XLTEK Protektor with its' integral current MEP stimulator was used for a small number of cases during the latter part of data collection.

TcMEPs

TcMEP stimulation is delivered via two disposable corkscrew electrodes (C1, C2) placed over the motor cortex of either hemisphere. Exact locations are halfway between Cz and C3/C4 and 2 cm anteriorly for C1/C2, respectively. The positions Cz, C3, and C4 are measured according to the International 10:20 Measurement System [4].

MEP responses are recorded using pairs of disposable stainless steel needle electrodes placed subdermally, in muscle sites proximal and distal to the surgery. We routinely opt to use Tibialis Anterior, Abductor Hallucis, and Quadriceps distally for TcMEP monitoring while proximal muscle groups such as Abductor Pollicis Brevis or Abductor Digiti Minimi are used for TcMEP validation. Other or additional muscle groups may be used if necessary.

The stimulating parameters used to stimulate the motor cortex and thus, elicit the MEPs varies depending on the IONM machine used due to the voltage versus current stimulus delivery. MEPs recorded using the Viking Select and the D185 are generated by a train of four pulses of stimulus intensities between 400 and 700 V, with an interstimulus interval (ISI) of 2 ms, delivered twice on each polarity (C1–C2, C2–C1). MEPs performed using the XLTEK Protektor utilizes its' integral current stimulator. Trains of 7–9 pulses, of 0.5–1 ms duration with an ISI of 3 ms, typically 160–200 mA intensity are also delivered twice on each polarity. In the instances when MEPs cannot be elicited using the standard C1–C2 positions, stimulation is delivered using C3–C4/C4–C3.

The stimulus level is increased until all responses are achieved and are supra-maximal. Once the stimulus intensity is established, it remains unchanged. Amplitude measurements are taken from the contra-lateral muscles. At the time the study data collection took place, we considered an absent response a significant change. We do not use bite blocks at present however this practice is currently under review with the introduction of the ANS/BSCN IOM guidelines created in 2013 which "recommend their use during MEPs".

Somatosensory evoked potentials

In addition to lower limb SSEPs, upper limb SSEPs are recorded not only to detect surgical changes in cases involving higher levels of surgery but also to detect ischemic changes due to patient positioning.

Supra-maximal stimulation for SSEPs is delivered via re-useable, surface Ag/AgCl EEG electrodes placed bilaterally over the Posterior Tibial and Ulnar/Median nerves. Stimulus intensity is typically between 20 and 40 mA, at rates between 4.7 and 6.9 Hz, 0.2–0.3 ms duration. Transmission responses are recorded simultaneously using disposable sticky Ambu Neuroline electrodes placed bilaterally over the popliteal fossa and brachial plexus (upper limb SSEPs).

Cortical, sub-cortical, and cervical responses are recorded using disposable corkscrew electrodes placed at Cz, Fz, C3, and C4 and disposable Ag/AgCl electrodes placed over the cervical spine.

Continuous averaging for 500 sweeps constitutes one run. Baseline values (signal amplitudes) are calculated post-diathermy and are taken as an average of ten runs. A reduction in signal amplitudes to 50 % of baseline values is deemed as a significant SSEP change.

Cerebral function analysing monitor

Cerebral Function Analysing Monitor (CFAM) is recorded continuously throughout surgery using the RDM CFAM 4. This records a single channel of EEG (looking at frequencies and amplitudes) using two disposable corkscrew electrodes placed over modified P4 and P3 electrode positions, providing real-time continual EEG monitoring.

Results

During the period between 2006 and 2013, 449 consecutive patients underwent spine deformity corrective surgery requiring IONM. The medical notes of all patients were reviewed and 12 (2.7 %) patients were identified to have suffered seizures pre-operatively forming an "at risk group" (Table 1). The mean age of the patients was 23 (9–59) years. There were 7 females. Eleven patients underwent scoliosis correction (4 neuromuscular, 1 degenerative, 6 idiopathic adolescent) and one had a sagittal balance correction procedure.

The operating surgeon was consulted regarding the use on TcMEP in any 'at risk' patient. In every case the value of TcMEP monitoring (earlier alerts, greater sensitivity to potential cord ischemia, etc.) were deemed to outweigh any perceived disadvantages.

IONM was performed continuously throughout surgery apart from during diathermy (the mean duration of the surgery was 7 h (ranging from 5 to 11 h)). Standard IONM protocol dictates four runs of lower limb SSEPs alternating with four pulses of MEPs (two pulses on either polarity) with one run of upper limb SSEPs occurring every 30 min.

Intra-operatively, there were no reported IONM alerts in any of the "at risk group", no bite-related tongue lacerations or broken teeth. There were no changes on the CFAM throughout any of the cases. Post-operatively, the mean in-hospital stay was 12 (4–25) days with no reported seizures during that period. At a mean follow-up of 23 (12–49) months post-discharge, none of the patients reported worsening of seizures (pattern or frequency) or required an alteration in their seizure-related medications.

Discussion

IONM was the natural by-product of a need for a continuously updated picture of the neurologic state in patients undergoing a significant operative spinal manipulation. The Stagnara wake-up test was first described in 1973 to allow for a "snap shot" assessment of motor function [6]. During the test, the neuromuscular blockade was reversed while the patient remained intubated but awake and asked to move his limbs. Although it is still in use, the wake-up test is associated with risks such as inadvertent extubation, post-operative recall, loss of intra-operative position, and the lack of sensory feedback [7]. Additionally, it is performed at a point following the correction completion, which means that identifying the point at which a neurologic injury took place might not be recognized.

The introduction of SSEPs reduced the need for a wake-up test [8]. While SSEPs reduced the risk of permanent neurological deficit [9], the technique was only able to reflect the function of the sensory pathway. This resulted in the reporting of a number of false-negative cases with catastrophic weakness sparing the sensory function [2]. Additionally, concerns were raised over the time lag between the cause and the identification of the effect of a surgical intervention, which was reported to be as long as 5 min [10]. More recently, TcMEPs were introduced in 1998 [11], and were shown to be an effective and safe monitoring modality in a variety of spine procedures including degenerative cervical spine surgery [10], pediatric deformity surgery [2, 12], and adult deformity correction surgery [13]. In a multi-center review, the monitoring records of a standardized multi-modality IONM (SSEP and TcMEP) of 1121 patients undergoing surgical correction for adolescent idiopathic scoliosis (AIS) in four centers were compared. Alerts were flagged in 34 (3.4 %) of the patients with 45 % only identified on the TcMEP. Moreover, of the 9 patients who woke up with a neurological deficit, 7 had a pure motor deficit, which was not identified by SSEP on four occasions [2]. A retrospective review of multi-modality IONM data (SSEP, TeMEP, EMG) collected on 102 patients managed surgically for adult deformity corrective surgery reported 5 cases with

Table 1 Pre-operative description of the "at risk group"

Patient number	Age (years)	Pre-operative diagnosis	Curve type	Major curve magnitude	Type of epilepsy
1	41	Cervicothoracic kyphosis	NA	NA	Idiopathic generalized
2	34	AIS	1-A-N	45	Idiopathic generalized
3	16	AIS	1-C-N	69	Idiopathic generalized
4	24	AIS	1-B-N	67	Idiopathic absence seizures
5	59	Degenerative lumbar deformity	NA	40	Idiopathic generalized
6	14	AIS	5-C-N	52	Tuberous sclerosis
7	12	AIS	5-C-N	55	Idiopathic generalized
8	18	Neuromuscular scoliosis	6-C-N	95	Idiopathic generalized
9	9	Neuromuscular scoliosis	6-C-N	78	Rhett's syndrome
10	17	AIS	1-B-N	91	Idiopathic generalized
11	11	Neuromuscular scoliosis	1-B-N	76	Noonan's syndrome
12	21	Neuromuscular scoliosis	6-C-Neg	91	Landau-Kalhner syndrome

AIS adolescent idiopathic scoliosis. Curve type based on Lenke's [5] classification

neurological deficit. The authors reported SSEP sensitivity at 33 %, no false negatives with TcMEPs and an overall sensitivity of the combined multi-modality IONM at 100 %, specificity 84.3 %, PPV 13.9 %, and NPV 97 % [13]. Similarly, an IONM review of 427 patients undergoing anterior cervical decompression and fusion confirmed TcMEP to be 100 % sensitive and specific compared to SSEPs (25 and 100 %, respectively) [10].

With TcMEP, a number of possible complications were reported including bite injuries (0.2 %—most common), scalp burns, cardiac dysrhythmias, and seizures [14, 15]. However, a clear cause and effect between TcMEP and cardiac dysrhythmias or seizures is yet to be confirmed [14]. Electrical stimulation of the brain can result in a clinical seizure based on a number of factors including stimulus characteristics (stimulus intensity, frequency, and duration), anesthesia, and the patient's predisposition (age, gender, history of epilepsy, brain lesions) [16, 17]. Seizure-inducing current amplitude thresholds (ranging from 36 to 869×10^3 μC) were identified to be 2–3 orders of magnitude above the maximum TcMEP [17]. As for current frequency, a review of the results of 68 studies including 2915 subjects reported no seizures during low-frequency single pulse or very brief high-frequency pulse train MEP monitoring (including direct, electrical and magnetic stimulation) [16]. Additionally, some anesthetic agents have also been shown to have "pro-convulsant" properties during the perioperative period such as enflurane, etomidate, ketamine, propofol, and fentanyl [18, 19]. This makes identifying the root cause of a seizure in such cases difficult.

While concerns about the "rare" occurrence of seizures with TcMEP is based on unpublished data [16], surgeons have largely avoided the use of TcMEP in patients with a history of active seizures to avoid the morbidity associated with triggering one [7]. A survey of 39 centers managing spinal deformity requiring IONM found that most centers opted not to use TcMEP with any of the following: history of seizures, a prior craniotomy or skull fracture, a metallic implant in the head, or an implanted stimulator (e.g., cochlear implant or cardiac pacemaker) [20]. In contrast, the Scoliosis Research Society (SRS) published an information statement for its members in 2009 in support of multi-modal monitoring in deformity spine surgery and reiterated Schwartz et al.'s conclusions on the safety of TcMEP even in the presence of cardiac disease, pacemakers, and a history of epilepsy [2, 15]. Our findings, despite the small "at risk" sample size, also supports the safety of TcMEP for monitoring patients with a history of seizures. TcMEP does not appear to trigger intra-operative or post-operative seizures and is not associated with deterioration in the seizure control in patients suffering from seizures pre-operatively. On balance, we believe the benefits of using TcMEP (namely increased monitoring sensitivity and earlier detection of neurologic deterioration) to outweigh the theoretical risk of a possible seizure trigger with transcranial stimulation.

Conflict of interest None.

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